REMARKS

Claims 1, 4, 6, 7, 10-14, 17, and 21-27 are pending. Claims 1, 4, 6 and 23 are withdrawn as directed to a non-elected invention.

The claims have been editorily amended to refer to SEQ ID NOS, as required by the Examiner. In addition, claims 1, 4, 6, 7, 11, 13, and 17 have been amended to recite that the primers hybridize under high stringency conditions, as supported at least in the paragraph bridging pages 7-8. New claims 23-27 recite specific high stringency conditions as supported at least in the paragraph bridging pages 7-8.

No new matter is added.

A. Restriction/Election Requirements

Applicant elected the invention of Group II, i.e., primer Claims 7-17 (now Claims 7, 10-14 and 17, and new Claim 22) without traverse. However, Applicants request rejoinder of method Claims 1-6 (now Claims 1, 4 and 6) upon allowance of the elected invention.

In addition, Applicants elected species iii, i.e., *Pythium* species without traverse; and the primer pair, IXa-IXb (SEQ ID Nos 17-18) with traverse. The Examiner has agreed to examine complementary primers IVa-IVb (SEQ ID Nos 7-8), and for this, the Examiner is thanked.

Applicants remind the Examiner that the Election of Species stated that upon allowance of the elected species, Applicants will be entitled to consideration of additional species.

Furthermore, Applicants request reconsideration of this requirement to the extent that the following primers be examined together with IXa/b: Ib, IIb, IIIb, Va/b, VIb, VIIb, VIIIb, and Xa/b, in addition to IVa/b, already rejoined. As previously noted, these primers make up Group B identified in the attachment to the Response to Restriction Requirement filed December 6, 2007. The primers of Group B are unified by virtue of their binding to a small region of DNA within the rRNA gene, the DNA sequence of which is not conserved between *Pythium* species (i.e., priming in this region can lead to species-specific amplification by PCR) but which falls between two highly-conserved regions (the regions in which generic primers G2 and G4 bind,

respectively). Furthermore, each primer set is specific to a *Pythium* sub-species that is a root vegetable pathogen, e.g. responsible for cavity spot in carrots.

B. Claim Objections

In paragraph 3, on page 3 of the Office Action, the Examiner rejects Claim 7, 10-14, 17 and 22, because SEQ ID numbers are not provided.

In view of the amendments to the claims, this rejection has been overcome.

C. Claim Rejections - 35 U.S.C. § 112, second paragraph

In paragraph 4, on page 3 of the Office Action, the Examiner objects to Claims 7, 10-14, 17 and 22 under 35 U.S.C. § 112, second paragraph.

Specifically, the Examiner objects to the expression "which hybridizes to" without reciting the hybridization conditions.

This rejection is overcome by amending the claims to recite that the hybridization is under high stringency conditions. Applicants assert that one of ordinary skill in the art could readily recognize whether hybridization conditions are high stringency conditions. Thus, the amended claims are not indefinite. The Examiner's attention is also directed to new claims 21-27, which recite specific parameters of the high stringency conditions.

D. Claim Rejections - 35 U.S.C. § 103

1. On page 4 of the Office Action, the Examiner rejects Claims 7, 10 and 13-14 under 35 U.S.C. § 103 as being unpatentable over Matsumoto et al in view of Buck et al.

Specifically, it is the Examiner's position that Matsumoto et al teaches a sequence which comprises sequences that are 100% homologous to primer SEQ ID NO:17 and its complement primer SEQ ID NO:7, as well as primer SEQ ID NO:18 and its complement primer SEQ ID NO:8. It is the Examiner's position that it would have been *prima facie* obvious, in view the sequences of Matsumoto et al, to design the claimed primers in view of the teachings of Buck et al, which allegedly teaches equivalency of primers.

For the following reasons, Applicants respectfully traverse the Examiner's rejection. The Examiner has stated that:

> "Regarding claims 7, 10, and 13-14, Matsumoto, C., Kageyama, K. and Suga, H. teach [sic] sequence of a region that comprises sequences that have 100% sequence homology to the claimed primers of SEQ ID No 17 and its complement SEQ ID No 7 as well as SEQ ID No 18 and its complement SEQ ID No 8."

Matsumoto *et al.* relates to an analysis of the rDNA of various Pythium species. It should be noted that the **only** DNA sequences which are **specifically** disclosed in Matsumoto *et al.* are the ITS primers (page 1334, column 2, under "RFLP analysis of rDNA-ITS region") and 7 oligonucleotide primers in Table 2 (page 1336). It can be seen therefore that Matsumoto *et al.* **does not teach** any of the primers of the invention or primers that hybridize to them.

The Examiner has specifically cited Accession no. AB1080008. This is a 907bp DNA sequence which is stated as covering the *P. sylvaticum* genes for ITS1, 5.8S rRNA and ITS2. **The only sequence that is specifically disclosed in this Accession no. is this 907bp sequence.**

The Examiner states:

> "Note the sequences of all of the above primers [are] 21 (SEQ ID No 17 and 7) and 20 (SEQ ID No 18 and 8) bases long.
>
> As indicated above Matsumoto et al. teach the region of Pythium species that encompasses the regions that are claimed as primers of the instant invention".

Whilst Matsumoto *et al.* does refer to the ITS-rDNA region of Pythium, neither Matsumoto *et al.* nor the 907bp sequence cited by the Examiner teach or suggest any of the primers of the invention or primers that hybridize thereto. The primers of the invention are 18-24mers; none of these is taught or suggested in any way in Matsumoto *et al.* or the 907bp sequence.

To say that a 907bp sequence "teaches" a 18-24mer is akin to saying that the complete sequence of the human genome "teaches" each of the individual genes. This is simply not correct.

The Examiner states:

> "Regarding claim 7, Matsumoto et al. teach an 18- to 24-mer oligonucleotide ...".

This is not correct. As shown above, Matsumoto *et al.* does not teach or suggest any 18- to 24-mer oligonucleotides of the invention.

The Examiner states:

> "Regarding claim 10, Matsumoto et al. teach the primer as claimed in claim 7 ...".

This is not correct. As shown above, Matsumoto *et al.* does not teach or suggest any 18- to 24-mer oligonucleotides of the invention.

The Examiner states:

> "Regarding claim 13, Matsumoto et al. teaches a primer composition comprising a pair of 18-24-mer oligonucleotide primers ...".

This is not correct. As shown above, Matsumoto *et al.* does not teach or suggest any 18- to 24-mer oligonucleotides of the invention.

The Examiner states:

> "Regarding claim 14, Matsumoto et al. teach the primer composition as claimed in claim 13 ...".

This is not correct. As shown above, Matsumoto *et al.* does not teach or suggest any 18- to 24-mer oligonucleotides of the invention.

The Examiner states:

> "It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have used the sequences of Matsumoto et al. to design the primer claimed in instant application as SEQ ID No 17 and 18 for detection of SEQ ID No 7 and SEQ ID No 8".

The Examiner goes on to cite the recent Supreme Court decision in KSR International Co. v. Teleflex Inc. (82 127 SCt 1727 (2007). The aforementioned decision refers to the possible obviousness of combinations **if**:

"... there is a design need or market pressure to solve a **problem** and there are a **finite number of identified, predictable solutions** ..." (emphasis added).

With regard to the **problem** to be addressed, Matsumoto *et al.* relates to an analysis of 47 isolates of *P. irregulare* in order to classify them taxonomically. It does not relate to the problem addressed by the current invention, i.e. the detection of pathogenic Pythium species in samples of soil or vegetables.

In this case, the choice of a 20mer primer from a sequence of 907bp would involve a selection from one of 887 possible primers. Further, there is no teaching or suggestion in Matsumoto *et al.* towards any one primer of the invention.

Furthermore, as stated above, Matsumoto *et al.* only specifically **identifies** two ITS primers and 7 other primers. None of these primers is relevant to this invention.

Additionally, and perhaps most importantly, it was not **predictable** whether any of the possible 887 primers would provide a solution to the problem addressed by the current invention.

Consequently, the findings of KSR International Co. v. Teleflex Inc. are not relevant to the instant invention.

The Examiner continues:

> "The sequence of Pythium rDNA-interspecific region (ITS regions) are taught to one of ordinary skill by prior art ...".

Whilst it is accepted that this ITS region and its sequence were known, Matsumoto *et al.* relates to "Intraspecific DNA polymorphisms of *Pythium irregulare*". This document relates to the use of the ITS region in order for taxonomic purposes to assign families to 47 isolates of *P. irregulare.* It does not address the problem which the instant invention addresses.

The Examiner states:

> "Since the claimed primers/probes simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers ...".

The Examiner is reminded that Matsumoto *et al.* **does not teach** and **does not suggest** any specific regions of the ITS-rDNA as being useful for primers.

The Examiner refers to the disclosures of Buck *et al.* (1999) Biotechniques 27: 528-536. Buck *et al.* relates to the design of DNA sequencing primers. In this document, the only issue is how to design DNA **sequencing** primers. This issue has no relevance to the instant patent application. The instant application does not relate to the highly controlled environment of DNA sequencing primers; it relates to primers that work in species-specific PCR in soil or vegetable samples.

In DNA sequencing, the only DNA that is included in the DNA sequencing reaction is the fragment to be sequenced and the primer. The fragment can be a PCR product, a purified plasmid, or it can even be a purified genomic DNA from one single organism (one species or one strain, clone or bacterial colony). Consequently, there is no surprise that any random primer would work in the DNA sequencing reaction.

In diagnostics or species-specific DNA, the situation is completely different. The template in a diagnostic PCR may be a complex mixture of DNA from hundreds, thousands or millions of different organisms. The primers of the invention were designed to work in this complex environment.

Accordingly, Applicants respectfully submit that the present invention is not taught or suggested in Matsumoto et al alone or in view of Buck et al, and thus request withdrawal of the Examiner's rejection.

2. Claims 11-12, 17 and 22 are rejected under 35 USC 103(a) as being unpatentable over Matsumoto *et al.* (2000) Mycol. Res. 104 (11):1333-1341 in view of Buck *et al.* (1999) Biotechniques 27: 528-536, further in view of Inoko *et al.* (WO 01/92572 A1 - with English equivalent document US 2003/0228585 A1).

Regarding claims 11-12, it has been shown above that neither Matsumoto *et al.* nor Buck *et al.* teach or suggest any 18-24mer primers of the invention or sequences that hybridize thereto.

Regarding claims 12, 17 and 22, it has been shown above that Matsumoto *et al.* does not teach or suggest any 18-24mer primers of the invention or sequences that hybridize thereto.

The teachings of Inoko *et al.* are therefore not relevant to the current invention.

Regarding claims 17 and 22, the Examiner states:

> "Matsumoto et al. teach a method of detecting fungal infection of soil or vegetables by pathogenic Pythium species (see Matsumoto et al. page 1333 par. 1 and Table where pathogenic Pythium species from vegetables and soil are described ...".

Matsumoto *et al.* page 1333, first paragraph, relates merely to the "Introduction" to the paper and a general background discussion of Pythium fungi. Neither this passage nor the teaching of Matsumoto *et al.* when taken in its entirety teach or disclose any of the primers of the invention or the use of these primers in detecting pathogenic fungi.

The Examiner states that:

> "It would have been prima facie obvious to one of ordinary skill at the time that the invention was made to package the primers of Matsumoto et al. and Buck et al. useful for detecting Pythium species in the kit format taught by Inoko et al. ..."

As pointed out above, there is no teaching or suggestion in Matsumoto *et al.* or Buck *et al.* towards the specific primers of the invention or primers which hybridize thereto.

It is respectfully asserted therefore that the subject matter of the instant claims is non-obvious over the disclosures of Matsumoto *et al.*, either alone or in combination with the disclosures of Buck *et al.* and/or Inoko *et al.*

3. Experimental data

The instant invention provides a set of oligonucleotide primers which are specific to pathogenic Pythium species, particularly those species that are responsible for the carrot disease cavity spot.

These primers can be used to test a soil or vegetable sample for the presence of such Pythium species, thus enabling a farmer to decide whether or not to treat a field with pesticides, whether or not the farmer should actually use that field to grow carrots, whether or not the field should be harvested for immediate consumption or could be stored with lower risk to develop the disease.

The Examiner has asserted:

> "It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have used the sequences of Matsumoto et al. to design the primer claimed in instant application as SEQ ID No 17 and 18 for detection of SEQ ID No 7 and SEQ ID No 8".

In order to address this assertion, one of the inventors has used a standard primer selection program to select primers from within the ITS region of *P. sylvaticum* cited by the Examiner (Accession no. AB108008). The species specificity of these primers was tested using a number of different Pythium species. The experimental details, results and discussion thereof are set out in the unexecuted Declaration under 37 C.F.R. § 1.132 submitted herewith. (The corresponding executed Declaration will be filed shortly.)

The data in Experiment A of the attached Declaration shows that these primers were **not** specific for pathogenic Pythium that are capable of producing cavity spot in carrots (i.e. *P. sulcatum*, *P. violae*, *P. sylvaticum*, *P. intermedium* and a new Pythium species that not yet has been given a name, "*P. vipa*").

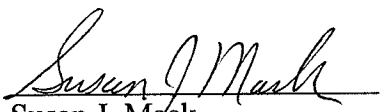
Additionally, Experiment B shows that the addition of a small number of nucleotides at the 5' or 3' end of SEQ ID NO: 18 reduces the species specificity of the primer. This further highlights the precision with which the primers of the invention were selected.

It is respectfully asserted therefore that this Declaration further supports the non-obviousness of the subject matter of the instant claims.

In view of the amendments to the claims and the arguments set forth above, reexamination, reconsideration and allowance are respectfully requested.

The Examiner is invited to contact the undersigned at the below listed number on any questions which might arise.

Respectfully submitted,



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